REMARKS

I. The Office Action

Claims 11-35 and 47-74 were withdrawn from consideration. The Office objected to claims 1-10 and 36-46 for failing to recite the full term for "HGF." Claims 1-8 were rejected under 35 U.S.C. § 101 for assertedly being directed to non-statutory subject matter. Claims 1-7 and 10 were rejected under 35 U.S.C. § 102(b) as assertedly being anticipated by Weimar et al., *Exp. Hematology*, *26*(9), 885-894 (1998) ("Weimar"), supplemented by Peled et al., *Science*, *283*, 845-848 (1999) ("Peled"). The Office rejected claims 1-3 and 5-10 under 35 U.S.C. § 102(b) for assertedly being anticipated in view of International Patent Publication No. WO 02/50263 ("Forbes"). Claims 1-10 and 36-46 were rejected under 35 U.S.C. § 103(a) for assertedly being obvious in view of Kollet et al., *Blood*, *97*(10), 3283-3291 (2001) ("Kollet"), taken in view of Weimar, Forbes, Devine et al., *Exp. Hematology*, *29*, 244-255 (2001) ("Devine"), and Shi et al., *Haematologia*, *92*, 897-904 (2007) ("Shi"). Reconsideration of these rejections is respectfully requested.

II. Pending Claims and Claim Amendments

Claims 1-10 have been cancelled. Applicants reserve the right to present claims to the same subject matter in related applications. Claims 11, 19, 27, 36, 47, 51, 56, 61, 62, 71, and 73 have been amended to recite "hepatocyte growth factor," thereby addressing the Office's objection to claims 36-46. The claim amendments are supported by the specification at, e.g., page 3, lines 24-28. No new matter has been added by way of the amendments. Claims 11-74 are pending, and claims 36-46 are currently under examination.

III. The Rejections Under 35 U.S.C. §§ 101 and 102(b) Are Moot.

The Office rejected claims 1-8 under Section 101 for assertedly being drawn to non-statutory subject matter, and claims 1-10 under Section 102(b) for assertedly being anticipated by Weimar, supplemented by Peled, and/or Forbes. The rejections are moot in view of the cancellation of claims 1-10.

IV. The Rejection Under 35 U.S.C. § 103(a) Should Be Withdrawn.

The Office rejected claims 1-10 and 36-46 under Section 103(a) for assertedly being obvious in view of Kollet, taken with Weimar, Forbes, Devine, and Shi. Solely in an effort to advance prosecution of the instant application, claims 1-10 have been cancelled. The rejection of claims 36-46 is traversed because the cited references fail to teach or suggest each limitation of the claimed method, and one of ordinary skill would not have combined the teachings of the references as asserted by the Office.

Claims 36-46 are directed to a method of generating stem cells suitable for transplantation. The method comprises (a) collecting stem cells; (b) exposing the stem cells to HGF or an active portion thereof; and (c) isolating stem cells having CXCR4 levels above a predetermined threshold, to thereby generate stem cells suitable for transplantation. Kollet purportedly discloses collecting CD34+ stem cells, treating cells with SCF, and transplanting cells in mice. The reference fails to teach or suggest, however, exposing stem cells to HGF or an active portion thereof, or isolating stem cells having CXCR4 above a predetermined threshold after exposure to HGF, as recited in steps (b) and (c), respectively, of claim 36. According to the Office, Kollet discloses "a method of isolating $CD34^+/CD38^-/CXCR4^+$ HSCs [hematopoietic stem cells] by flow cytometry (FACS) after treating $CD34^+/CD38^-$ or $CD34^+/CD38^{-/low}$ HSCs with SCF and IL-6 (see Material and Methods)." (Office Action, page 6.) On the contrary, Kollet reports that SCF induces CXCR4 expression, but does not teach or suggest isolating cells with increased CXCR4 levels for transplantation. Weimar, Forbes, Devine, and Shi do not cure the deficiencies of Kollet in this regard. Weimar and Forbes assertedly disclose exposing $CD34^+$ cells to HGF, and Devine assertedly reports that mesenchymal and hematopoietic stem cells have similar homing properties. The Shi reference was published in 2007, is not prior art to the instant application, and cannot be used as the basis of an obviousness rejection. Moreover, none of the cited references available under Section 103 teach or suggest step (c) of the presently claimed method and, for this reason alone, the obviousness rejection should be withdrawn.

In addition, one of ordinary skill would not have been motivated to modify the teachings of Kollet to replace SCF with HGF. The Office contends that Weimar discloses exposing $CD34^+$ stem cells to HGF, and a person of ordinary skill "would recognize the

benefit of HGF and would use the HGF for the preparation of HSCs suitable for transplantation." (Office Action, pages 6-7.) The Office further asserts that Weimar teaches that SCF has proliferative and adhesion properties similar to that of HGF, and it would have been obvious to combine SCF and HGF to promote proliferation, adhesion, and cell survival. (Office Action, pages 6-7.) The Weimar reference, however, teaches that combining SCF and HGF *does not* act synergistically to promote, e.g., cell survival. SCF was reported to be the more potent survival factor, and addition of HGF did not enhance survival of treated cells. (Weimar, paragraph bridging pages 889-890.) In addition, Weimar teaches that incubation of stem cells with HGF alone *failed* to induce colony formation, while exposure to SCF increased the number of stem cell clusters. (Weimar, page 888, first full paragraph; Figure 2.) No synergistic effect was observed on colony formation when HGF was combined with SCF. (*Id.*) Given the advantages of SCF disclosed in Weimar, one of ordinary skill would not have been motivated to modify the teachings of Kollet to use HGF. Moreover, the disclosure in Forbes of HGF as an anti-fibrolytic agent expressible by stem cells would not lead an ordinarily skilled artisan to modify the teachings of Kollet.

One of ordinary skill also would not have been motivated to combine HGF with SCF, as proposed by the Office, given the lack of additive or synergistic effect achieved by the combination. The Office cites *In re Harza*, 274 F.2d 669 (C.C.P.A. 1960), as supporting its assertion that "duplicating components with similar functions within a composition is obvious." In *Harza*, the only distinction between a claimed material for joining gaps between concrete slabs and similar material disclosed in the prior art was a plurality of ribs on each side of the claimed material. *Id.* at 774. The plurality of ribs was not deemed to be a patentable distinction over the disclosure of a single rib because "mere duplication of parts has no patentable significance unless a new and unexpected result is produced." *Id.* Combination of SCF and HGF is not a "mere duplication of parts" in the same vein as *Harza*; the cytokines have different functions *in vivo* and different effects on stem cells, as illustrated by Weimar. In the absence of evidence of synergistic effect, one of ordinary skill would not have been motivated to combine HGF and SCF as asserted by the Office.

For the reasons set forth above, the cited references do not render obvious the subject matter of claims 36-46. More particularly, Kollet fails to disclose or suggest isolated stem cells, and none of the secondary references remedies this defect. Further, Shi is not available as art against the pending claims. Further, none of the references, considered alone or in any combination, teaches or suggests step (c) of the claimed method, which is expressly recited in claim 36. In addition, one of skill would not be motivated to substitute HGF for SCF because these are different proteins with different functions yielding different effects. Thus, the Office's reliance on *Harza* is misplaced. Accordingly, Applicants respectfully request withdrawal of the Section 103(a) rejection.

V. Conclusion

In view of the above amendments and remarks, Applicants believe that the pending application is in condition for allowance. The Office is invited to contact the undersigned attorney by telephone if there are issues or questions that might be efficiently resolved in that manner.

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Respectfully submitted,

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